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Amendment and Response

Serial No.: 10/694,385

Confirmation No.: 5758

Filed: October 27, 2003

For: METHODS FOR CREATING A COMPOUND LIBRARY AND IDENTIFYING LEAD CHEMICAL
TEMPLATES AND LIGANDS FOR TARGET MOLECULESRemarks

The Office Action mailed June 26, 2006 has been received and reviewed. Claims 18 and 29 having been amended, and claims 1-17, 21, and 31-45 having been canceled, without prejudice, the pending claims are claims 18-20 and 22-30. Reconsideration and withdrawal of the rejections are respectfully requested.

The 35 U.S.C. §112, First Paragraph, Rejection

The Examiner rejected claim 29 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner objected to claim 29 because it recites a specific numeric dissociation constant when there is no specific target structure or specific structure of a compound that binds to the target. This is respectfully traversed.

The claims of the present application are directed to an NMR method for identifying a compound that binds to a target molecule by collecting relaxation-edited NMR spectra. As such, there is no need to specify any specific structures of any specific compounds. A significant advantage of the claimed NMR method is the use of it in a system to identify a test compound that binds to a target molecule, wherein the concentration of target molecule and each test compound in each sample reservoir is no greater than about 100 μ M. As such, no specific structures of compounds need be recited. That is, these claims are directed to a method and an advantageous aspect of the method, not to any specific compounds *per se*.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claim 29 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner objected to claim 29 for allegedly omitting essential steps. This is respectfully traversed; however in the interest of expediting

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prosecution, claim 29 has been amended according to the Examiner's suggestion.

The 35 U.S.C. §103 Rejection

The Examiner rejected claims 18-30 under 35 U.S.C. §103 as being unpatentable over Hajduk et al. (*J Am Chem Soc.*, 1997;119:12257-12261) and in view of Keifer (*Drugs of the Future*, 1998;23(3):301-317). This rejection is respectfully traversed.

Applicants have developed a method that involves the use of a relaxation-editing binding assay based on NMR spectroscopy that eliminates the need to develop a high-throughput functional assay, and also allows the method to be used on molecular targets lacking a known function.

One important element that contributes to the success of Applicants' method is selection of a suitable library of compounds, which is neither taught nor suggested by the cited documents. That is, the combination of Hajduk et al. and Keifer does not teach or suggest that the nature of the plurality of mixtures of test compounds is important in successfully implementing the claimed method. Applicants have selected specific test compounds ("wherein each test compound has a solubility in deuterated water of at least 1 mM at room temperature") that can be used effectively at relatively low concentration ("wherein the concentration of target molecule and each compound in each sample is no greater than 100 μ M"). This is another important element that contributes to the success of Applicants' method. Carrying out the binding assay at such low concentrations (and preferably near equimolar ratios of target molecule and test compounds, as recited in claim 27) contributes to the identification of compounds with similar affinity and avoids detection of unwanted compounds that are less specific in their binding and harder to turn into lead chemical templates (see, e.g., Applicants' specification at page 10, line 19 through page 11, line, 3).

It is respectfully submitted that the following advantages are not appreciated by either Hajduk et al. or Keifer or the combination thereof: the water solubility of the test compounds ("at least 1 mM") and the preferred low molecular weight ("no greater than

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350 grams/mole," as recited in claim 22) contribute to a chemical library with compounds that are more likely to be "lead-like" and more likely to provide successful downstream drug-design projects (see, e.g., the specification at page 10, lines 5-18).

Although Hajduk et al. may disclose specific test compounds having the desired solubility, and the desired concentrations of target molecule and test compounds, there is no teaching or suggestion that these are important features that contribute to the success of Applicants' method. Recognition of these as important features to utilize in the system of Keifer does not come absent hindsight. Even then, this recognition only occurs when one uses the information provided by Applicants' application, which is inappropriate.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure. This burden has not been met by the Patent Office. Withdrawal of the rejection is respectfully requested.

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It is respectfully submitted that the pending claims 18-20 and 22-30 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted

By

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August 31, 2006

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CERTIFICATE UNDER 37 CFR §1.8:

The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 31st day of August, 2006, at 5:19 PM (Central Time).

By: Sara E. Wigant
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